

What is claimed is:

1. A composition of matter for inhibiting specific gene expression with reduced side effects, the composition comprising a modified CpG-containing phosphorothioate oligonucleotide that is complementary to a portion of a genomic region or gene for which inhibition of expression is desired, or to RNA transcribed from such a gene.

10 2. The composition of matter according to claim 1, wherein the modified CpG is selected from alkylphosphonate CpG, inverted CpG, 2'-O-substituted CpG, 5-methylcytosine CpG, stereospecific phosphorothioate CpG, phosphotriester 15 CpG, phosphoramidate CpG and 2'-5' CpG.

20 3. A method for modulating gene expression in a mammal with reduced side effects comprising administering to the mammal a composition of matter according to claim 1, wherein the oligonucleotide is complementary to a gene that is being expressed in the mammal.

25 4. A method for therapeutically treating, with reduced side effects, a disease caused by aberrant gene expression, the method comprising administering to an individual having the disease a composition of matter according to claim 1, wherein the oligonucleotide is complementary to a gene that is aberrantly expressed, wherein such aberrant expression causes the disease.

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